1. Name of the Medicinal Product

TachoComb® H

2. Qualitative and quantitative composition of the active substances

1 cm^2 TachoComb® H fleece contains:

Human Fibrinogen	5.5 mg
Human Thrombin	2.0 IU
Bovine Aprotinin	0.071 Ph.Eur U
Equine Collagen	2.1 mg

3. Pharmaceutical form

Collagen sponge coated with thrombin, fibrinogen and aprotinin

4. Clinical particulars

4.1 Therapeutic indications

For local application only.
To use as supportive treatment to improve haemostasis

4.2 Posology and method of administration

4.2.1 Posology

The dose is determined by the size and shape of the wound and must be individualised by the treating physician. In clinical trials the average dose has been 1-2 patches (9.5 cm x 4.8 cm); application of up to 7 patches has been reported. For smaller wounds, e.g. in minimal invasive surgery the smaller size sheets (4.8cm x 4.8 cm or 3.0 cm x 2.5 cm) are recommended. The sheets can be cut to the correct size and shape if too large. Rests of the fleece not needed should be discarded.

4.2.2 Method of administration

TachoComb® H is used under sterile conditions. Prior to application the wound area should be largely cleansed (e.g. from blood, disinfectants and other fluids). TachoComb® H is applied locally to the wound surface with the yellow tinted side against the wound. After removal of TachoComb® H from the sterile package the patch should be premoistened in saline solution and then applied immediately to the bleeding/leaking surface. TachoComb® H should then be pressed gently to the wound for 3-5 minutes. The TachoComb® H fleece should be used in a way that also 1-2 cm beyond the margins of the wound is covered. If more than one sheet is used the sheets should overlap.

ATTACHMENT A

4.3 Contra-indications

Strong (arterial and/or venous) bleeding
Known hypersensitivity to bovine aprotinin or other constituents of the product.

4.4 Special warnings and special precautions for use

Only for local application!

TachoComb® H comes in sterile packages and must be handled accordingly. Use only flawless packages. Post-sterilisation is not possible.

As with any protein product, allergic type hypersensitivity reactions are possible. If signs of hypersensitivity reactions (see section 4.8) occur, the administration has to be discontinued immediately.

This product contains bovine protein (aprotinin). Especially after repeated application of aprotinin there is an increase in risk for allergic reactions, therefore any use of aprotinin or aprotinin-containing products should be documented.
In case of shock, the current medical standards for shock treatment are to be observed.

Virus Safety:
When medicinal products prepared from human blood or plasma are administered, infectious diseases due to the transmission of infective agents cannot be totally excluded. This applies also to pathogens of hitherto unknown nature. The risk of transmission of infective agents is however reduced by:

- selection of donors by a medical interview and screening of donations for the three major pathogenic viruses HIV, HCV, HBV;
- testing plasma pools for the absence of HCV genomic material;
- removal/inactivation procedures included in the production process that have been validated using model viruses and are considered effective for HIV, HCV, HBV. The viral removal/inactivation procedures may be of limited value against non-enveloped viruses such as HAV or parvovirus B19.

4.5 Interactions with other medicinal products and other forms of interactions

No formal interaction studies have been performed.

4.6 Pregnancy and lactation

The safety of TachoComb® H for use in human pregnancy or breastfeeding has not been established in controlled clinical trials. Experimental animal studies are insufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and postnatal development.
Therefore, TachoComb® H should be administered to pregnant and lactating women only if clearly needed.

4.7 Effects on ability to drive and use machines

Not applicable (as there is no systemic use).

4.8 Undesirable effects

As is also the case with fibrin sealants, hypersensitivity or allergic reactions (which may include angioedema, chills, fever, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) may also occur in rare cases after application of TachoComb® H. In isolated cases, these reactions may progress to severe anaphylaxis. Hypersensitivity reactions may especially be seen, if the preparation is applied repeatedly or administered to patients known to be hypersensitive to bovine proteins or other constituents of the product.

4.9 Overdose

There is no experience of overdose.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group:
Haemostyptics/antihaemorrhagics (ATC code: B02B C)

Pharmacodynamics

TachoComb® H contains fibrinogen and thrombin in solid form as a coating on the surface of a collagen sponge. At contact with physiological fluids, e.g. blood, lymph or physiological saline solution, the components of the coating dissolve and partly diffuse into the wound surface. This is followed by the fibrinogen-thrombin reaction which initiates the last step of blood coagulation. Fibrinogen is converted into fibrin monomers which spontaneously polymerise to a fibrin clot. Thereby the collagen sponge is tightly glued to the wound surface, resulting in air and liquid tight sealing. The fibrin thus formed is then crosslinked by endogenous factor XIII, creating a firm, mechanically stable network with good adhesive properties. Aprotinin is added to TachoComb® H to prevent excessively rapid fibrinolysis.

5.2 Pharmacokinetic properties

In animal studies the collagen sheet shows a progressive degradation. 24 weeks after application only a few remnants were present without any signs of local irritation. The fibrin clot is degraded by fibrinolysis and phagocytosis.

5.3 Preclinical safety data

Toxicological properties

Single dose toxicity studies in different species of animals have shown no signs of acute toxic effect.

6. Pharmaceutical particulars

6.1 List of excipients

Human Albumin, L-Arginine Monohydrochloride, Sodium Chloride, Trisodium Citrate, Riboflavine (E 101) to mark the coated side.

6.2 Incompatibilities

None.

6.3 Shelf life

3 years.
Once opened, TachoComb® H should be used immediately.

6.4 Special precautions for storage

TachoComb® H should be stored in refrigerator (2-8°C).

6.5 Nature and contents of container

TachoComb® H is packed in a double packaging:

An outer container consisting of an aluminium-bonded foil sachet
An inner container (sterile) consisting of a polystyrene blister sealed with a peel lacquer-laminated paper.

Package with 1 sponge of 9.5 cm x 4.8 cm
Package with 2 sponges of 4.8 cm x 4.8 cm
Package with 1 sponge of 3.0 cm x 2.5 cm
Package with 5 sponges of 3.0 cm x 2.5 cm

7. Marketing Authorisation Holder

Nycomed Pharma GmbH
Fraunhoferstrasse 7
D-85737 Ismaning b. München
Phone: (089)96281-0
Fax: (089)96281-444

8. Marketing Authorisation Number

9. Date of first Authorisation / Renewal of the Authorisation

10. Date of Revision of the Text

Summary of Product Characteristics

1. Name of the medicinal product
TACHOCOMB absorbable wound dressing

2. Qualitative and quantitative composition
1 cm^2 of 0.5 cm-thick TachoComb-fleece contains:

collagen from horse tendons	1.3 - 2.0 mg
coated with:	
human fibrinogen	4.3 - 6.7 mg
bovine thrombin	1.5 - 2.5 I.U.
bovine aprotinin	0.055 - 0.087 Ph.Eur.U.

3. Pharmaceutical form
coated dry foam fleece

4. Clinical particulars

4.1 Therapeutic indications
TachoComb should be used in particular in cases where hemorrhages or biliary, lymphatic, liquor or aerial fistulae cannot be controlled by conventional methods or if the results expected by these methods are insufficient.

TachoComb is suited for the hemostasis and tissue conglutination, especially during surgical interventions in parenchymatous organs, as e.g. in the liver, spleen, pancreas, kidneys, lungs, adrenals and thyroid gland, lymph nodes; it can also be used to stop hemorrhages during surgical interventions in the ENT-region, in gynecology, urology and in the vascular and bone surgery (e.g. taking of spongiosa), traumatology, etc.

TachoComb can also be used for the prophylactic treatment of lymphatic, biliary and liquor fistulae. Also air leakages occurring during surgical interventions in the lungs can be sealed with TachoComb.

4.2 Posology and method of administration
Dosage
Dosage depends on the size of the wound to be covered. The TachoComb fleece should be used in a way that also 1 - 2 cm beyond the margins of the wound are covered. If more than one fleece is required to cover the wound, they should be applied to overlap each other. TachoComb can be cut to the desired size with sterile scissors before and after it is applied to the wound area.
Rests of the fleece not needed should be discarded.

Form of application
To be applied on surgical wound areas.

4.3 Contraindications
Hypersensitivity to the constituents.

4.4 Special warnings and precautions for use
The build-up of antibodies against bovine thrombin is reported for various bovine thrombin preparations – especially after repeated application and/or after application of high doses. In such cases where chemical laboratory tests use bovine thrombin to evaluate thrombin time, a distinct prolongation in thrombin time is shown.
When the test is repeated using human thrombin as a reagent, the thrombin time is usually normal.
TachoComb comes in sterile packages and must be handled accordingly. Use only flawless packages. Post-sterilization is not possible.

4.5 Interaction with other medicinal products and other forms of interaction
No formal interaction studies have bee performed.

4.6 Pregnancy and lactation
Use during pregnancy and lactation period is possible, however, accurate diagnosis is imperative.

4.7 Effects on ability to drive and use machines
Not applicable (as there is no systemic use).

4.8 Undesirable effects
Hypersensitivity or allergic reactions may occur after application of TachoComb in rare cases.

4.9 Overdose
Not applicable.

5. Pharmacological properties

5.1 Pharmacodynamic properties
Pharmaco-therapeutic group:
Haemostyptics/antihaemorrhagics (ATC: B02B C)
Sealant (ATC: V03AK)

Pharmacodynamics
TachoComb contains fibrinogen and thrombin in solid form as a coating on the surface of a collagen fleece. At contact with physiological fluids, e.g. blood, lymph or physiological saline solution the components of the coating dissolve and partly diffuse into the wound surface. This is followed by the fibrinogen-thrombin reaction which initiates the last step of blood coagulation. Fibrinogen is converted into fibrin monomers which spontaneously polymerise to a fibrin clot. Thereby the collagen fleece is tightly glued to the wound surface. The fibrin thus formed is then crosslinked by endogenous factor XIII, creating a firm, mechanically stable network with good adhesive properties.

5.2 Pharmacokinetic properties
In animal studies the collagen sheet shows a progressive degradation. 24 weeks after application only a few remnants were present without any signs of local irritation. The fibrin clot is degradated by fibrinolysis and phagocytosis.

5.3 Preclinical safety data
Single dose toxicity studies in different species of animals have shown no signs of acute toxic effect.

6. Pharmaceutical particulars

6.1 List of excipients
Riboflavin (E101)

6.2 Incompatibilities
None.

6.3 Shelf life
36 months

6.4 Special precautions for storage
To be stored at refrigerator temperatures (2 to 8° C).

6.5 Nature and contents of container
An outer container consisting of an aluminium-bonded foil sachet

An inner container (sterile) consisting of a polystyrene blister sealed with a peel lacquer-laminated paper.

1 piece, 5 x 1 and 10 x 1 piece (multi-packages)
Size of fleece: 9.5 x 4.8 x 0.5 cm
1 piece, 3 x 1 piece (multi-packages)
Size of fleece: 2.5 x 3 x 0.5 cm
2 pieces
Size of fleece: 4.8 x 4.8 x 0.5

6.6 Instructions for use and handling
TachoComb is used under sterile conditions. Prior to application the wound area should be largely cleansed (e.g. from blood, disinfectants and other fluids).

The coated side (yellow marking) of the collagen fleece is applied to the wound area and pressed onto it for 3 - 5 min. When applied to sufficiently wet wounds TachoComb does not need any additional wetting. When applied to dry wound surfaces TachoComb should be treated before with physiological NaCl-solution so to obtain adhesion to the dry wound surfaces.
Wetted TachoComb fleeces must be used instantly! It is advisable to remove blood and secreted fluids from surgical gloves and instruments before the use of TachoComb so that the fleece does not stick to them.

7. Marketing authorisation holder
Nycomed Austria GmbH, Linz, Austria

8. Marketing authorisation number

9. Date of first authorisation/Renewal of the authorisation

10. Date of revision of the text

11. Dispensing

CE 0408 STERILE R

Gebrauchsinformation

Tachotop®

1. Bezeichnung des Medizinproduktes

Tachotop®

Natives, resorbierbares Kollagen aus Kollagenfibrillen vom Pferd

2. Indikationsgruppe

Hämostyptika

3. Anwendungsgebiete

Als Wundauflage zur lokalen Blutstillung in der operativen Medizin; Auskleidung von Gewebedefekten, Hautersatz bei epidermalen/dermalen Läsionen; Füllung von Knochendefekten, z.B. nach Zystektomien oder Entfernung verlagerter bzw. retinierter Zähne.

4. Gegenanzeigen

Absolute Kontraindikationen:

- Überempfindlichkeit gegen Kollagen
- Intravasale Anwendung
- Anwendung in infizierten Bereichen

Erkenntnisse über Risiken der Anwendung während der Schwangerschaft und Laktation liegen nicht vor. Eine durch Kollagen bedingte Beeinflussung ist unwahrscheinlich.

5. Nebenwirkungen

Gelegentlich kommt es zu Schmerzen nach Auflegen eines trockenen Vlieses auf die Wundfläche. In Einzelfällen kann es zu Unverträglichkeitsreaktionen gegen Kollagen kommen, die in Abhängigkeit von ihrem Schweregrad ärztlich behandelt werden müssen.

6. Wechselwirkungen mit anderen Mitteln

Antiseptika, die Chlor freisetzen (z. B. Chloramin) sowie Tannin und Kaustika, die Proteine verändern, dürfen nicht gemeinsam mit Tachotop® angewendet werden.

Salben und Puder sowie Silikonpräparate können die Zwischenräume des Kollagenvlieses verändern, so daß sie nicht gemeinsam mit Tachotop® appliziert werden sollen.

7. Art und Dauer der Anwendung

Falls erforderlich, kann Tachotop® mit trockener, steriler Schere auf die gewünschte Größe zugeschnitten werden.

Tachotop® kann trocken oder feucht angewendet werden. Die Wunde wird von Blut gereinigt und ein entsprechendes Stück Tachotop® wird rauhe und durch kurzes Andrücken aufgelegt. Die Wunde sollte zur Blutstillung nicht übermäßig mit Tachotop® ausgepolstert werden. Obwohl Tachotop® im Wundbett bzw. an feuchten (sezernierenden) Flächen gut haftet, kann gegebenenfalls die Befestigung mit Situationsnähten günstig sein.

Zum Auffüllen von Knochendefekten im Kieferbereich wird das in kleine Quader geschnittene Kollagenvlies mit Blut durchtränkt und druckles schichtweise eingebracht.

8. Wirksamkeit und biologische Eigenschaften

8.1 Wirkmechanismus

In Übereinstimmung mit der physiologischen Funktion körpereigener Kollagenfibrillen für die Blutstillung haben und aggregieren angeschwemmte Thrombozyten an den Fibrillen des Tachotop®, und aktivieren die Blutgerinnung. Nach abgeschlossener Blutstillung gibt das räumliche Gitterwerk des Tachotop® einem Keagel erhöhte Festigkeit.

Die am Kollagengerüst haftenden Thrombozyten zerfallen und setzen die prokoagulatorischen Plättchenfaktoren PF3 und PF4 frei.

NYCOMED

Tachotop®

Natives, resorbierbares Kollagen aus Kollagenfibrillen vom Pferd

2 x 1 Vlies

9,5 x 5 cm

Lokales Hämostyptikum

Zum Einbringen in Wunden und als Wundauflage

CE 0408

STERILE R

NYCOMED

ATTACHMENT C

Über die blutstillende Wirkung hinaus ist der fördernde Effekt von Kollagenpräparaten auf die Vorgänge der Wundheilung, wie sie sich an jede Blutstillung anschließen, nachgewiesen.

8.2 Biologische Sicherheitsdaten

Tierexperimentelle Untersuchungen an Hunden ergaben, daß Kollagen tierischen Ursprungs die Heilung von Hautläsionen nicht beeinträchtigt, sondern fördert. Eine Stimulation der Zellaktivität, insbesondere der Fibroblastenaktivität wird beschrieben.

8.3 Abbau des Produktes

Implantiertes Kollagen tierischen Ursprungs wird in der Regel innerhalb von 2 bis 6 Wochen resorbiert. Die Resorption erfolgt durch eingewanderte Makrophagen und durch Kollagenase.

Kollagen ist ein hochmolekulares Protein, das die Plazenta- und Blut-Hirnschranke nicht passiert.

9. Hinweise für den Gebrauch

Wegen der besonderen Affinität von Kollagen zu blutenden und sezernierenden Wundflächen kann Tachotop® auch an Instrumenten und OP-Handschuhen haften, die mit Blut in Berührung gekommen sind. Dies läßt sich durch vorheriges Befeuchten des Instrumentariums bzw. der Handschuhe mit physiologischer NaCl-Lösung vermeiden.

10. Dauer der Haltbarkeit

5 Jahre

11. Besondere Lager- und Aufbewahrungshinweise

Trocken aufbewahren.

Tachotop® ist steril verpackt und dementsprechend zu handhaben. Nach Öffnen der Verpackung ist das Präparat sofort zu verwenden. Nur unbeschädigte Packungen dürfen verwendet werden. Eine (Re-)Sterilisation ist nicht möglich.

Tachotop® darf nach Ablauf des auf der Packung angegebenen Ablaufdatums nicht mehr angewendet werden.

12. Darreichungsformen und Packungsgrößen

Tachotop®
Packung mit 2 x 1 Vlies zu je 9,5 x 5 cm: EAN 9003638119015
Packung mit 2 x 3 Vliesen zu je 5 x 3 cm: EAN 9003638119039

13. Hersteller

NYCOMED Austria GmbH
St.-Peter-Str. 25
A-4020 Linz

7811804
0209
0-1402

28/04 '05 DO 08:02 FAX +43 732 6919 4443 R&D PRODUCT MAINTENANCE 001

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